PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12319730/TDO/FT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/001150**	International Filing Date *(day/month/year)* 4 September 2003	Priority Date *(day/month/year)* 4 September 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] A61K 38/04, 39/00; A61P 37/02

Applicant

MONASH UNIVERSITY et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☒	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
2 April 2004	20 December 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **ANTHONY MURFETT** Telephone No. (02) 6283 2243

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001150

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	20-21, 39-42	YES
	Claims	1-19, 22-38, 43-45	NO
Inventive step (IS)	Claims	20-21, 39-42	YES
	Claims	1-19, 22-38, 43-45	NO
Industrial applicability (IA)	Claims	1-45	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

This opinion has considered the following documents cited in the International Search Report:

D1 WO 2001/029081 A

D2 Reinelt S et al

D3 Guichard G et al

D4 WO 2002/092120 A

D4 was published prior to the international filing date but later than the claimed priority date but which would otherwise be considered to be of particular relevance. These documents will not be commented on in this report but may be considered relevant during national phase examination. See Box VI for further information.

D1 discloses modified peptides, wherein the modifications can comprise a β-amino acid substitution and their use as agonists of T cells. The document also discloses T cell recognition of a β-amino acid substituted peptide through a Major Histocompatability Complex (MHC)-peptide complex on the surface of antigen presenting cells (PBMCs) and assays to screen the functional activity of β-amino acid substituted peptides. The document further discloses the use of the agonistic modified peptides to induce tolerance in patients with autoimmune diseases. See abstract, Tables 2-3 pages 34-35, examples 15-16.

D2 discloses MHC-I restricted peptide epitopes which have been modified with β-amino acid substitutions and their use as T cell receptor antagonists. This document further discloses the ability of the β-amino acid substituted peptides to bind to MHC-I and recognition of the β-amino acid substituted peptides by allogenic T cells through a MHC-peptide complex. The document also discloses an assay to screen for the functional activity of β-substituted amino acid peptides. See abstract, Table I, methods.

D3 discloses a modified melanoma peptide which have been modified with β-amino acid substitutions and their enhanced binding capacity to MHC-I. This document further discloses the ability of the β-amino acid substituted peptides to be recognised by T cells through MHC-peptide complexes. An assay to screen for the functional activity of β-substituted amino acid peptides is also disclosed. See abstract, Table I, methods.

Continued in Supplementary Box I

Supplemental Box I
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

Novelty and Inventive Step

Claims 1-2 and dependent claims encompass the use of β-amino acid substituted peptides to modulate (agonise or antagonise) the T cell response, via contacting the T cell through a MHC-peptide complex

Claims 20, 40 and dependent claims encompass a method of agonising a T cell response or enhancing an inadequate T cell response by co-administering an antagonistic β-amino acid substituted peptide with an non-substituted peptide.

Claims 21, 39 and dependent claims encompass a method of antagonising a T cell response or reducing an unwanted T cell response by co-administering an agonistic β-amino acid substituted peptide with an non-substituted peptide.

Claims 22, 43 and dependent claims encompass a method of treating an aberrant, unwanted or otherwise inappropriate peptide specific T cell response by administering an agonistic or antagonistic β-amino acid substituted peptide. It is noted that an inappropriate immune response, includes an inadequate (or minimal) immune response, see page 43 of the instant application.

Claim 44 encompasses a pharmaceutical composition comprising a β-amino acid substituted peptide in a carrier.

Claim 45 encompasses a method of designing and screening for β-amino acid substituted peptide analogues.

The invention defined in claims 1-19, 22-38, 43-45 are not novel or inventive in light of D1-D3. These documents disclose β-amino acid substituted peptides, their use to agonise or antagonise the T cell response, their use to treat aberrant, unwanted or inappropriate responses and assays to screen for their functional activity. In light of claim 44, β-amino acid substituted peptides are well known, with D1-D3 being only an example of the prior art. It is also noted that the features defined in the dependent claims do not add any features which are considered to be novel or inventive. For this reason the invention defined in claims 1-19, 22-38, 43-45 and dependent claims are not novel or inventive.

The invention defined in claims 20-21, 39-42 are considered to be novel and inventive in light of D1-D3. There is no disclosure or suggestion in D1-D3 of a method of agonising a T cell response or enhancing an inadequate T cell response by co-administering an antagonistic β-amino acid substituted peptide with an non-substituted peptide **or** a method of antagonising a T cell response or reducing an unwanted T cell response by co-administering an agonistic β-amino acid substituted peptide with an non-substituted peptide. In light of claims 21, 39, even though D1 discloses the use of agonistic modified peptides to induce tolerance in a model of DTH (delayed type hypersensitivty) (ie use an agonist to reduce an unwanted response), there is no **enabling disclosure** of co-administration of the β-amino acid substituted peptide and a non-substituted peptide to induce tolerance. Therefore the invention defined in claims 20-21, 39-42 is considered novel and inventive.

Industry Applicability

Claims 1-45 are considered to be Industrially Applicable.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
D4 P,X WO 2002/092120 A	21 November 2002	14 May 2002	15 May 2001

D4 anticipates claims 1-2, 22, 43-45 and dependent claims of the instant invention. D4 discloses modified peptides that bind to HLA molecules (MHC molecules), wherein the modifications can comprise a β-amino acid substitution. The document further discloses the enhanced antigenicity and immunogencity of such modified peptides (ie discloses an agonistic action). See abstract, Table IA-Table IB pages 19-22, page 8 paragraph 4, claims.

With regard to the document(s) listed in Box VI under "certain documents cited", these are documents published prior to the international filing date but later than the priority date claimed but which would otherwise be considered to be of particular relevance.

Under the PCT, novelty is considered only in respect of documents published before the priority date. The relevance of a document published after the priority date is dependent upon national law. Such documents are excluded from consideration in preliminary examination, under the PCT Guidelines but have been included here for information.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 44 is not fully supported by the description. There is only support for β-amino acid substituted peptides that are able to **modulate the T cell response** via recognition through a MHC-peptide complex. The inventive concept appears to be that peptides that are recognised by T cells when substituted with β-amino acids are able to modulate (antagonise or agonise) the T cell response. However as currently drafted the claims are not limited to the inventive concept, merely encompassing any β-amino acid substituted peptide. This goes beyond the disclosure of the invention described in the description and therefore claim 44 does not define the invention described in the description.

Claim 45 is not fully supported by the description. There is only support for a method for designing and screening for β-amino acid substituted peptide analogues **that modulate the T cell response** relative to the T cell response inducible by a non-substituted form of said peptide. The inventive concept appears to be that peptides that are recognised by T cells when substituted with β-amino acids are able to modulate (antagonise or agonise) the T cell response. However as currently drafted claim 45 is not limited to this feature and therefore does not define the invention described in the description.

Claim 20 is unclear because the claim omits that the peptide to be presented to said T cells, is to be presented in the context "**of an MHC-peptide complex**", c/f claim 21.